KARTAGENER'S SYNDROME- CASE SERIES

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ABSTRACT

BACKGROUND

It is an autosomal recessive genetic disorder. It consists of triad of situs inversus, chronic sinusitis and bronchiectasis. In this syndrome, there is defective movement of cilia leading to recurrent chest, ENT infections and infertility. We hereby report five cases of this syndrome. The need for early detection of the condition is important, so that whenever possible, options for timely treatment of infertility can be offered.

MATERIALS AND METHODS

All patients with dextrocardia who came to our Institute from 2015 to 2017 with history of cough with sputum were included in our study. Detailed history was taken, and proper clinical examinations were done in all patients. Radiological and biochemical tests were done and correlated with patient's outcome. All patients were treated according to our Institutional protocol.

RESULTS

There are five cases included in this study, in which 3 are males and 2 are females. Among the females, one is adult of age 48 years and another is 22 years old young adult. Among the 3 males included, one is preadolescent of age 11 years and the other two are young adults of ages 20 years and 18 years.

CONCLUSION

The patients with Kartagener's syndrome suffers from repeated infections of chest, ear, nose and throat, but infertility should also be evaluated in these patients and if possible, assisted reproductive techniques should be advised, so that they can be offered with a suitable option to have children.

KEY WORDS

Bronchiectasis, Kartagener's Syndrome, Sinusitis, Situs Inversus.

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BACKGROUND

Kartagener's syndrome is a type of ciliary motility disorder called primary ciliary dyskinesia. It is an autosomal disorder of ciliary motility characterised by chronic lung disease, rhinosinusitis, hearing impairment and subfertility. It comprises a triad of situs inversus, bronchiectasis and sinusitis. The prevalence of PCD is about 1 in 10,000, but it is more common in populations where consanguinity is common. The impaired ciliary motility of Kartagener's syndrome is responsible for the recurrent chest and ear, nose, throat (ENT) and sinus infection and infertility. The early diagnosis is important for the preservation of pulmonary function and improvement of the quality of life in the patients.

Case Reports

Case 1

This is a 48-year-old non-smoker female born to non-consanguineous parents. She presented to outpatient clinic in October 2016 with chief complaints of cough with yellowish mucoid sputum for the previous 10 years with recurrent episodes of common cold, sneezing since 10 years, exertional shortness of breath associated with wheezing which was more during winter months and which was relieved with bronchodilators. The patient also revealed that she frequently developed headache, nasal blockade, cough and running nose since her childhood. She attained menopause at 46 years of age before which she had regular 4 - 5 cycles per month.

At the time of first visit, the vital parameters were within normal limits. Physical examination revealed grade 3 clubbing. Sinus tenderness was present on maxillary region. On auscultation, coarse crepts were heard on bilateral infra-

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axillary, axillary, bilateral infrascapular and bilateral mammary areas, diffuse scattered wheeze is present all over the chest. Patient also had history of infertility; however, she was not evaluated for that due to her financial constraints.

Blood investigations of complete blood picture revealed leucocytosis with increased neutrophils. Chest x-ray PA view showed dextrocardia with aortic knuckle on right side. Electrocardiogram showed the evidence of dextrocardia. HRCT chest revealed dextrocardia and cystic and saccular bronchiectatic changes in all segments of RLL, anterior, superior lingular and inferior lingular of left upper lobe, and basal, post basal and lateral basal segments of left lower lobe. USG abdomen revealed situs inversus totalis.

CT PNS revealed chronic sinusitis of bilateral maxillary and ethmoidal sinuses, bilateral CSOM. A 2D echo revealed moderate PAH, dextrocardia with normal EF with right-sided aortic arch. PFT revealed moderate obstruction with reversibility and there is no impairment of functional status as assessed by 6 MWT. Saccharin test is 1 hour and 30 minutes. The patient is still in follow-up with maintenance therapy and LTOT and treated for exacerbations.

Case 2

This is a 22 years female, non-smoker of non-consanguineous parents presented to OP clinic in (March 2017) with chief complaints of cough with yellowish mucoid sputum for the previous one month with recurrent cold associated with progressive increase in shortness of breath since three years.

Her past history was significant, in that she had frequent visits for recurrent chest infections. Her family history revealed no consanguinity.

At the time of visit, vital parameters were normal. Physical examination was normal except for pallor. On auscultation, early inspiratory crepts were present on left infrascapular and right infraaxillary and axillary regions and scattered wheeze was present.

Chest x-ray PA view revealed dextrocardia with aortic arch is towards right side. Electrocardiogram revealed dextrocardia. HRCT chest revealed dextrocardia and bronchiectatic changes involving left "middle lobe" with situs inversus. CT-PNS revealed maxillary sinusitis.

A 2D echo-dextrocardia with right-sided aortic arch and mild PAH. USG Abdomen: Situs inversus totalis.

Spirometric evaluation revealed evidence of mild obstruction and with no impairment of functional status as assessed by 6MWT. Saccharin test revealed 1 hour 30 mins of sensation of taste.

The patient is still in follow-up to prevent exacerbation. Pneumococcal vaccination (PPSV23) and therapy with MDI with fixed dose of Formoterol-Fluticasone was given.

Case 3

This is a 20 years non-smoker male, born to non-consanguineous parents who had nocturnal cough with slight whitish mucoid sputum and with epigastric pain, presented initially to general surgery department and was referred by them for further evaluation.

On further evaluation, the patient had history of recurrent attacks of cough and running nose with nasal congestion since his childhood and mild shortness of breath only on exertion.

Physical examination was normal. On auscultation crepts were heard on right infraaxillary and axillary and right mammary regions. On cardiac auscultation, heart sounds were heard on right side.

Chest x-ray PA view revealed dextrocardia with aortic arch on the right side. Electrocardiogram revealed dextrocardia. USG upper abdomen showed evidence of dextrocardia. HRCT chest revealed bronchiectatic changes in bilateral lower lobes of right middle lobe and left lingular segments and situs inversus total is with spleen on right side and liver on left side.

Spirometric evaluation is normal. Saccharin test revealed 1 hour and 15 minutes. CTPNS revealed sinusitis of bilateral maxillary sinusitis.

The patient had no functional impairment with normal 6MWT. Routine blood investigations were normal. Semen analysis for sperm motility was not performed, because the patient was unmarried and declined to do so.

The patient was advised regular follow-up and also bronchial hygiene and regular follow-ups, but he missed the follow-up visits.

Case 4

This is an 18-year-old male non-smoker, born to non-consanguineous parents. He presented to OP clinic with chief complaints of running nose since 15 days, cough with whitish mucoid sputum since 10 days with no shortness of breath. On further evaluation, the patient revealed that he had similar complaints since childhood with increased symptom in cold seasons. At the time of presentation, vitals were normal.

Physical examination was normal except sinus tenderness. Auscultation of respiratory system was normal. Heart sounds were heard on right side.

Chest x-ray PA view revealed dextrocardia, aortic arch is on right side. Electrocardiogram showed the evidence of dextrocardia. Spirometric evaluation was normal. HRCT revealed cylindrical bronchiectasis in the right middle lobe, lingula, bilateral centrilobular nodules and dextrocardia. CT PNS revealed sinusitis. USG abdomen revealed situs inversus. The patient had no functional impairment with normal six-minute walk test. Saccharin test was 1 hour. The patient declined to give the seminal sample for analysis. The patient is still in follow-up and was advised bronchial hygiene and advised regular follow-ups.

Case 5

This is an 11-year-old male child born to 3rd consanguineous parents, presented to paediatrics department with chief complaints of cough with whitish mucoid sputum, low-grade nocturnal continuous fever that progressed to high grade. The patient was referred by them for further evaluation.

Patient had recurrent cough and cold since the age of 5 years and was suffering from recurrent respiratory tract infection once in every 2 - 3 months.

Physical examination was normal. On auscultation, mild bilateral infrascapular crepts were heard. On cardiac auscultation, heart sounds were heard on right side.

Chest x-ray revealed dextrocardia with aortic arch on right side.

A 2D echo confirmed dextrocardia. USG upper abdomen showed the evidence of situs inversus totalis with spleen on right side and liver on left side. HRCT chest revealed bronchiectatic changes on right lower zone. CT-Paranasal sinuses showed right maxillary sinusitis with left maxillary polyp.

The patient's parents were advised regarding regular follow-up and also regarding bronchial hygiene.

DISCUSSION

The ciliary motility disorders are of two types, congenital and acquired. The congenital disorders are labelled as Primary Ciliary Dyskinesia (PCD). In nearly 50% of cases of Primary Ciliary Dyskinesia, patients have situs inversus. Such cases of PCD's with situs inversus are known as Kartagener's syndrome.⁽¹⁾

Primary ciliary dyskinesia is phenotypically and genetically a heterogeneous condition, wherein the primary defect is in the ultrastructures or function of cilia.^(2,3) Such defects are identified in approximately 90%⁽³⁾ of PCD patients and involve the outer dynein arms, inner dynein arms or both. 38%⁽³⁾ of the PCD patients carry mutations of the dynein genes, DNAI⁽⁴⁾ and DNAH5.⁽¹⁾

Occasionally, Kartagener's syndrome may be associated with reversible airflow obstruction.⁽⁵⁾

Diagnostic Criteria

The diagnostic criteria include⁽⁶⁾ the following and clinical picture is suggestive of recurrent chest infections, bronchitis, rhinosinusitis since childhood along with one or more of the following-

1. Situs inversus in patient or sibling.
2. Alive, but immotile spermatozoa.
3. Reduced or absent transbronchial mucociliary clearance.
4. If the cilia show characteristic ultrastructural defect on electron microscopy, apart from fulfilling the criteria mentioned above.

There are Two Types of Screening Tests done for Diagnosis of Primary Ciliary Dyskinesia. They are as follows-

- a. Exhaled nasal nitric oxide measurement test, which is usually low in PCD.
- b. Saccharin test: To know the mucociliary function of nasal epithelium.

Diagnostic Tests

The Diagnostic Tests are-

1. Ciliary beat pattern analysis.
2. Ciliary beat frequency analysis, which is done by video recording and electronic microscopic confirmation of ultrastructural ciliary defect.

Usually, the sample collection is by biopsy of nasal mucosa and laparoscopic biopsy of tubal mucosa as was done by Halbert et al.⁽⁷⁾ However, we could not perform these tests, and the diagnosis was essentially clinicoradiological with azoospermia and oligospermia (As a variant of Kartagener's syndrome). The issue of fertility was not addressed in the initial reports which were published by Arge.⁽⁸⁾ He postulated that 3 male patients are having immotile spermatozoa & infertility, while women presented with reduced fertility. The infertility of males is due to diminished sperm motility, while in females is due to defective ovum transport because of dyskinetic motion of oviductal cilia, suggesting that ciliated endosalpinx is essential for human reproduction.⁽⁹⁾

Recently, there is development of assisted reproductive techniques for rational treatment for these patients, and to date there have been reported pregnancies using subzonal insemination (SUZI) and intracytoplasmic sperm injection (ICSI).⁽¹⁰⁾

The case report of Kordus et al⁽¹¹⁾ shows that even in severe cases of asthenozoospermia, ICSI⁽¹²⁾ can overcome the inability of the spermatozoa to reach the ovum and produce healthy offspring. However, both SUZI and ICSI require expertise and is not available in all units and is a costly procedure.

The outcome⁽¹⁰⁾ of treatment should be individualised depending on sperm motility. In cases where there is no sperm motility, ICSI may be the most appropriate treatment. However, if sperm motility is present, a trial of in vitro fertilisation (IVF) should be considered.⁽¹⁰⁾

There is one drawback regarding the fertility treatment of men with PCD. The possibility that the resultant child has the risk of being affected by the same condition. It is therefore necessary to counsel the couples regarding the possibility of genetic risks. In those cases, follow-up of the children is also very important.⁽¹⁰⁾

CONCLUSION

The patients with Kartagener's syndrome suffers from repeated infections of chest, ear, nose and throat, but infertility should also be evaluated in these patients and if possible, assisted reproductive techniques should be advised so that they can be offered with a suitable option to have children.

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